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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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BAXTER HEALTHCARE CORPORATION
1 BAXTER PARKWAY
DF2-2E
DEERFIELD, IL 60015

EXAMINER	
FORD, ALLISON M	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 11/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/789,320	MARTIS ET AL.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,7,9,10,13-17,19,20 and 23-30* is/are pending in the application.

4a) Of the above claim(s) *10,13-17 and 26-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,7,9,19,20 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

In the reply filed 17 October 2005 applicants confirmed their election of Group I (claims 1-9 and 19-25) with traverse. The traversal is on the ground(s) that the amendment to independent claim 10 incorporates limitations found in independent claim 1, and now the method provided in claims 10-18 covers similar subject matter as in the claims of Group I, and thus the methods should be rejoined. This is not found persuasive because, though the amendment to claim 10 requires the reagent to be derived from a silkworm larvae plasma, and requires the peptidoglycan concentration to be about 10 ng/mL or less, the methods presented in claims 1 and 19 remain distinct from the method presented in claim 10. Specifically, the method of claims 1 and 19 require the addition of the silkworm larvae plasma directly to the glucose polymer for the purpose of detecting the amount of peptidoglycan associated with the glucose polymer; the method of claim 10 does not require a reaction between the glucose polymer and the silkworm larvae plasma, rather it is unclear how the silkworm larvae plasma reagent is to be utilized in the method. Therefore the methods remain patentably distinct because the silkworm larvae plasma reagent has a different use and different effect in each of the methods. The requirement is still deemed proper and is therefore made FINAL.

Amendments to claims 1, 5, 9, 10, 13, 19, 23, 24 and 25 have been entered. Claims 4, 6, 8, 11, 12, 18, and 21-22 have been cancelled. Claims 1-3, 5, 7, 9-10, 13-17, 19-20, and 23-30 remain pending in the current application. Claims 1-3, 5, 7, 9, 19, 20 and 23-25 have been examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5, 7, 9, 19-20 and 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's claim 1 and its dependents are directed to a method for manufacturing a peritoneal dialysis solution, comprising providing a glucose polymer; adding a silkworm larvae plasma (SLP) reagent to the glucose polymer wherein the SLP reagent reacts with peptidoglycan associated with the glucose polymer; determining an amount of the peptidoglycan associated with the glucose polymer; conducting a modified bioburden test on the glucose polymer for an acidophilic thermophilic organism that is a source of the peptidoglycan; and using the glucose polymer to make the peritoneal dialysis solution if it is determined that the peptidoglycan concentration of the glucose polymer is about 10 ng/mL or less.

Applicant's claim 19 and its dependents are directed to a method of testing a peritoneal dialysis solution for presence of a gram positive microbial contaminant that exceeds a level sufficient to cause peritonitis, comprising adding a silkworm larvae plasma reagent to a glucose polymer powder, wherein the silkworm larvae plasma reagent is capable of reacting with the peptidoglycans associated with the glucose polymer powder to initiate a serine protease cascade; conducting a modified bioburden test on the glucose polymer for an acidophilic thermophilic organism that is a source of the peptidoglycan and determining whether the peptidoglycan concentration exceeds about 10 ng/mL in the peritoneal dialysis solution and whether the peritoneal dialysis solution is sterile if the glucose polymer is used to make the peritoneal dialysis solution.

Both independent claims 1 and 19 require a modified bioburden test to be performed on the glucose polymer to test for the presence of an acidophilic thermophilic organism that is a source of the peptidoglycan; however applicant fails to provide sufficient written description of the modified bioburden

test or sufficient written description of all acidophilic thermophilic organisms that are a source of peptidoglycan that can be identified by the modified bioburden test. To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one of ordinary skill in the art can reasonably conclude that the inventor had possession of the claimed invention. In the instant case applicant has claimed testing for the presence of any acidophilic thermophilic organism by means of a modified bioburden test. Applicant's specification at pages 7 and 19 generally describes that the modified bioburden test is to be carried out at a pH of about 4-5 and a temperature of about 50-60°C in addition to at a pH of about 7.0 to 7.4 and at a temperature as described in various Pharmacopoeias; applicants have not provided specific parameters that would allow for detection of *any* and *all* acidophilic thermophilic organisms, including the numerous organisms that have yet to be isolated or discovered. Applicants describe a single acidophilic thermophilic organism, *Alicyclobacillus acidocaldarius* (See Spec Pg. 6), which may be contained in some natural products used to make icodextrin; while methods are known for the detection of *A. acidocaldarius*, discussion of a single acidophilic thermophilic organism is not sufficient to allow one of ordinary skill in the art to immediately envisage detection of any and all acidophilic thermophilic organisms which may be present in contaminated glucose polymers.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5, 7, 9, 19-20 and 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claim 1 and its dependents are directed to a method for manufacturing a peritoneal dialysis solution, comprising providing a glucose polymer; adding a silkworm larvae plasma (SLP) reagent to the glucose polymer wherein the SLP reagent reacts with peptidoglycan associated with the glucose polymer; determining an amount of the peptidoglycan associated with the glucose polymer; conducting a modified bioburden test on the glucose polymer for an acidophilic thermophilic organism that is a source of the peptidoglycan; and using the glucose polymer to make the peritoneal dialysis solution if it is determined that the peptidoglycan concentration of the glucose polymer is about 10 ng/mL or less.

Applicants' amended claim 1 remains unclear because the steps do not appear to be commensurate in scope with the purpose recited in the preamble. The preamble states the claim is drawn to a method of *manufacturing a peritoneal dialysis solution*, but the body of the claim involves steps intended to *test the peptidoglycan concentration of a glucose polymer*, for use in a peritoneal dialysis solution. Though the claim includes a step of "using the glucose polymer to make the peritoneal dialysis solution" this step is contingent on the peptidoglycan concentration, the glucose polymer solution can only be used *if the peptidoglycan concentration is about 10 ng/mL or less*; therefore, the claimed method is not a method for manufacturing a peritoneal dialysis solution, but rather for testing the suitability of the glucose polymer for use in a peritoneal dialysis solution. If the glucose polymer has a peptidoglycan solution that exceeds 10 ng/mL, the glucose polymer cannot be used for manufacture of the dialysis solution, and the claim would have no utility.

Amended claim 1 is further unclear because it is not clear how the amount of peptidoglycan is detected, it is not clear if the modified bioburden test is to detect the amount of peptidoglycan or the presence of the microorganism that produces the peptidoglycan. From the specification it appears that the reaction between the silkworm larvae plasma reagent (SLP reagent) and the peptidoglycan produces a detectable signal, which is to be detected by a colorimetric measurement (claim 7), and then a *further*

modified bioburden test is to be carried out in order to test for the presence of the microorganism which is a source of the peptidoglycan; however, this is not clear from the current claim language. Though the claims are read in light of the specification, limitations from the specification are not to be read into the claims. Additionally, under the interpretation that the peptidoglycan is detected via the reaction between the SLP reagent and the peptidoglycan, and a separate test comprising a modified bioburden test detects the presence of acidophilic thermophilic organisms, it is not clear how detection of the acidophilic thermophilic organisms relates to the method as claimed; as use of the glucose polymer depends solely on the concentration of peptidoglycan, not on the presence of any contaminating organisms.

Amended claim 1 is further unclear because it fails to particularly point out and describe the 'modified bioburden test' that is to be conducted on the glucose polymer. Applicant's specification at pages 7 and 19 generally describes that the modified bioburden test is to be carried out at a pH of about 4-5 and a temperature of about 50-60°C in addition to at a pH of about 7.0 to 7.4 and at a temperature as described in various Pharmacopoeias; however, these general ranges do not definitely define the specific 'modified' parameters necessary for the claimed 'modified bioburden test.' It is critical that the parameters be altered appropriately so as to identify the acidophilic and thermophilic organisms which are usually undetected at regular bioburden parameters; therefore because the modified ranges are critical, they must clearly be defined.

Applicant's claim 5 is indefinite because it is not clear if the colorimetric measurement is the modified bioburden test, or if it is a separate test used to determine the amount of peptidoglycan. In claim 1 it is not clear if the test to determine the amount of peptidoglycan is the modified bioburden test, or if it is a separate test; therefore dependent claims further describing these tests are unclear.

Applicant's claim 7 requires the silkworm larvae plasma reagent to be added to the peritoneal dialysis solution. It remains unclear how the silkworm larvae plasma reagent is added to the peritoneal dialysis solution when claim 1 requires the silkworm larvae plasma reagent to be part of the peritoneal

dialysis solution. Claim 1 requires the silkworm larvae plasma reagent to be added to the glucose polymer; thus it appears claim 7 intends to require the silkworm larvae plasma reagent to be added to the glucose polymer, which fails to further limit claim 1.

Applicant's claim 19 and its dependents are directed to a method of testing a peritoneal dialysis solution for presence of a gram positive microbial contaminant that exceeds a level sufficient to cause peritonitis, comprising adding a silkworm larvae plasma reagent to a glucose polymer powder, wherein the silkworm larvae plasma reagent is capable of reacting with the peptidoglycans associated with the glucose polymer powder to initiate a serine protease cascade; conducting a modified bioburden test on the glucose polymer for an acidophilic thermophilic organism that is a source of the peptidoglycan and determining whether the peptidoglycan concentration exceeds about 10 ng/mL in the peritoneal dialysis solution and whether the peritoneal dialysis solution is sterile if the glucose polymer is used to make the peritoneal dialysis solution.

Amended claim 19 remains unclear because the preamble does not appear to be commensurate in scope with the body of the claim. The preamble of claim 19 states the method is intended to test a peritoneal dialysis solution *for the presence of a gram positive microbial contaminant*; because only bacteria would be classified as gram positive or gram negative, it appears the step of conducting the modified bioburden test for the presence of an acidophilic thermophilic *organism* is the only step that accomplishes the claimed method. The steps relating to testing for the presence of peptidoglycan and determining the concentration of peptidoglycan do not fall under the scope of the preamble because peptidoglycan is not a 'gram positive microbial contaminant.'

Use of the phrase "level sufficient to cause peritonitis" in the 2nd-3rd lines of the claim renders the claim indefinite. The term "sufficient to cause peritonitis" is not specifically defined by the claim; though the claim later mentions a concentration exceeding about 10 ng/mL, it is not clear if this is considered a level sufficient to cause peritonitis. Therefore the claim remains indefinite.

Claim 19 is further unclear due to the term 'gram-positive microbial contaminant' because, as stated above, only bacteria are classified as gram-positive or gram-negative, therefore it is not clear what applicant is considering 'microbial contaminants.' Furthermore it is not clear how the final step 'determining whether a peptidoglycan concentration exceeds about 10 ng/ml in the peritoneal dialysis solution *and whether the peritoneal dialysis solution is sterile if the glucose polymer is used to make the peritoneal dialysis solution'* is accomplished, particularly with regards to the italicized portion the language is so confusing that it does not appear to involve a positive step.

Amended claim 19 is further unclear because it fails to particularly point out and describe the 'modified bioburden test' that is to be conducted on the glucose polymer. Applicant's specification at pages 7 and 19 generally describes that the modified bioburden test is to be carried out at a pH of about 4-5 and a temperature of about 50-60°C in addition to at a pH of about 7.0 to 7.4 and at a temperature as described in various Pharmacopoeias; however, these general ranges do not definitely define the specific 'modified' parameters necessary for the claimed 'modified bioburden test.' It is critical that the parameters be altered appropriately so as to identify the acidophilic and thermophilic organisms which are usually undetected at regular bioburden parameters; therefore because the modified ranges are critical, they must clearly be defined.

Applicant's claim 25 is indefinite because it is not clear what positive step is involved to test the peritoneal dialysis solution. It is not clear if an additional step is required, in addition to the steps outlined in claim 19, or if claim 25 is stating an intended purpose of one of the steps of claim 19.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5, 7, 9, 19-20 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gokal et al (Perit Dial Int, 2002), Martin et al (Advances in Peritoneal Dialysis, September 2003) and Goffin et al (Nephrol Dial Transplant, November, 2003), each in view of "Extraneal" Baxter (May 22, 2002), and Tsuchiya et al (FEMS, 1996), and further in view of Ashida et al (US Patent 4,970,152).

Gokal et al describe icodextrin as the colloid osmotic agent in peritoneal dialysates, commercially available as EXTRANEAL. At the time of the article use of icodextrin peritoneal dialysates was associated with an increased rate of sterile peritonitis. Gokal et al report that testing by the manufacturer revealed the icodextrin solutions were contaminated with peptidoglycan, a non-endotoxin, weak pyrogen contained in the cell wall of gram positive bacteria and fungi (See Gokal et al, pg. 447-448). Gokal et al report the manufacturer performed silkworm larvae plasma tests to identify peptidoglycan as the contaminant.

Similar reports by Martin et al and Goffin et al teach the manufacturer reported that the increased frequency of sterile peritonitis in peritoneal dialysis patients using icodextrin-containing dialysates was due to peptidoglycan contamination in certain batches of icodextrin-containing dialysates (See Goffin et al, Pg. 2483 & Martin et al, Pg. 193).

A letter released by Baxter (the manufacturer) teaches that the contaminated batches of icodextrin had a peptidoglycan level of >10 ng/mL (See "Extraneal" Letter, Baxter).

The silkworm larvae plasma test (SLP test) is used to detect peptidoglycans using the prophenol oxidase cascade; it can be used to detect microbial contamination. Silkworm larvae plasma contains all the factors of the prophenol oxidase cascade; when added to a sample suspected of containing peptidoglycan the peptidoglycan activates the prophenol oxidase cascade resulting in the production of melanin, which can be colorimetrically measured (See Tsuchiya et al, Pg. 131-134).

Therefore, Gokal et al disclose the use of the SLP test which involves addition of a silkworm larvae plasma reagent (which applicant calls a reagent in its raw material form) to an icodextrin-containing dialysate solution to test for the presence of peptidoglycan, which is indicative of gram positive bacteria contamination in the icodextrin-containing dialysate.

Though Gokal et al teach performing the SLP test on batches of peritoneal dialysis solution, and not the raw icodextrin, it would have been obvious to one of ordinary skill in the art at the time the invention was made to test the icodextrin before formulation of the complete peritoneal dialysis solution. One of ordinary skill in the art would have been motivated to test the raw icodextrin for peptidoglycan contamination before mixing the complete dialysis solution in order to reduce waste. For example, if the icodextrin was found to be contaminated, the tester would discard only the icodextrin, as opposed to formulating the complete dialysis solution, which comprises additional electrolytes and chemicals, then testing to find out the icodextrin was contaminated and having to discard the entire solution, thus wasting the additional electrolytes and chemicals. One would expect success testing a solution of pure icodextrin because the SLP test responds to the presence of peptidoglycan; it does not require additional reagents present in a complete dialysate.

Additionally, though Gokal et al do not report the concentration of peptidoglycan found in the contaminated icodextrin nor do they report an acceptable threshold level of peptidoglycan that can be tolerated in the peritoneal dialysate solution, Baxter reports that peptidoglycan levels in excess of 10 ng/mL were considered 'elevated' and were therefore recalled (See "Extraneal" Baxter); therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to test for peptidoglycan levels in excess of about 10ng/mL, as this was considered the threshold level by the Baxter distributors to initiate recall. Furthermore, because the SLP test produces melanin as an end product it would have been obvious to one of ordinary skill in the art to perform colorimetric measurements to determine the amount of peptidoglycan in the solution. Ashida et al teach a method to correlate melanin

production to peptidoglycan concentration by creating a standard curve using known amounts of peptidoglycan, and then comparing the experimentally obtained measurements (See Ashida et al, col. 12, ln 10-52). One of ordinary skill in the art would have been motivated to determine the concentration of peptidoglycan present in contaminated samples of icodextrin in order to determine if the level is acceptably low enough for safe distribution (>10ng/mL) (See, e.g. Ashida et al, col. 5, ln 20-29). One would have expected success quantifying the concentration of peptidoglycan in the solution because Ashida et al teach methods of colorimetrically determining the amount of peptidoglycan present in a sample.

Finally, it would further have been obvious to one of ordinary skill in the art at the time the invention was made to further test the potential glucose polymer for bacterial contamination because bacteria are the source of peptidoglycans which stimulate the sterile peritonitis (See Gokal et al, Martin et al, and Goffin et al). As submitted by applicant normal Pharmacopoeia testing standards test for bacterial contaminants at room temperature and at neutral pH (See Spec, Pages 5-6 & Response to Office Action Pg. 7, third full paragraph); however, in light of the increased sterile peritoneal outbreaks reported in 2002 one of ordinary skill in the art would have been motivated to perform increased testing on potential glucose polymer solution to test for presence of contaminating bacteria outside the range normally tested by Pharmacopoeia testing, such as acidophilic and/or thermophilic bacteria, such as *Alicyclobacillus acidocaldarius*. Means of testing for the presence and proliferation of acidophilic and/or thermophilic bacteria such as *A. acidocaldarius* were known in the art at the time the invention was made, see for example, Oita. Oita teaches various antimicrobial agents that can be useful against *A. acidocaldarius* and methods of testing for the presence of *A. acidocaldarius* after treatment with the antimicrobial agents (See Oita, col. 4, ln 29-col. 5, ln 16). Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to perform additional bacterial contamination tests (which applicant calls modified bioburden tests), in addition to the normal Pharmacopoeia tests, in order to detect presence of

acidophilic thermophilic bacteria, such as *A. acidocaldarius* that could be sources of peptidoglycans. One would have been motivated to perform the additional modified bioburden tests to ensure sterility in light of the recently contaminated stock supply of icodextrin, in order to prevent continued outbreaks of sterile peritonitis. One would have expected success testing for acidophilic thermophilic bacteria in the glucose polymer solution because means are known in the art to detect the presence of such bacteria (See, e.g. Oita).

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 17 October 2005 have been fully considered, but are not found persuasive. Specifically applicants argue that Gokal et al, Martin et al, and Goffin et al do not teach or suggest a threshold level of 10 ng/mL of peptidoglycan that can be tolerated in the peritoneal dialysis solution. Applicants further argue that none of the art cited in the prior action taught or suggested the testing for peptidoglycan (by SLP test) in addition to testing for acidophilic thermophilic bacteria (by a modified bioburden test). Applicants further argue that the examiner used hindsight reasoning to justify the combination and modification of the references in support of the obvious rejection.

In response to applicant's argument regarding the lack of teachings regarding the threshold level of peptidoglycan tolerable in peritoneal dialysis solutions, it is noted that the disclosure of the "Extraneal" product information release by Baxter has now been relied upon in the rejection. The product information release by Baxter teaches that batches of peritoneal dialysis solution with peptidoglycan levels of 10 ng/mL or more have been recalled in order to ensure patient safety; this submission provides motivation to consider 10 ng/mL peptidoglycan as the threshold for tolerable peptidoglycan levels.

In response to applicant's argument that the combination of SLP testing for peptidoglycan levels and modified bioburden testing for presence of acidophilic thermophilic bacteria is non-obvious over the prior cited art, it is noted that the new limitation prompted a new grounds of rejection. For the reasons stated above in the current rejection, it is asserted that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use SLP testing in addition to 'modified bioburden testing' in order to ensure quality and sterility in the icodextrin solutions provided.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The examiner has in fact not used hindsight reasoning as evidenced by the motivation and reasoning provided in the above rejections. The references relied upon provided motivation within themselves for combination and modification. Regarding optimization of the threshold level of peptidoglycan the examiner has currently relied upon the disclosure of the "Extraneal" product information release to support the optimization of the acceptable threshold level of peptidoglycan in peritoneal dialysis solution, see teachings above.

Conclusion

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 17 October 2005 prompted the new ground(s) of rejection presented in this Office action. See MPEP § 609.04(b). Additionally, applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. See MPEP § 706.07(a). Accordingly, **THIS**

ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651